

REMARKS

Reconsideration of the application in view of the above amendments and following remarks is respectfully requested.

Claims 1-59 were pending. In view of the restriction requirement or to enhance the clarity of the claimed invention, claims 1, 9, 18, 20, 29, 31, 40, 50 and 59 have been amended and claims 2, 11, 22, 33, 43 and 52 have been cancelled without prejudice. No new matter has been added. Therefore, claims 1, 3-10, 12-21, 23-32, 34-42, 44-51 and 53-59 are now pending in the subject application.

In the Office Action dated April 05, 2004, claims 1-59 were objected to as containing non-elected subject matter. Applicants affirm the election of Group I of the restriction requirement. As set forth above, certain claims have been amended and others cancelled to remove the non-elected subject matter.

Therefore, it is believed that the objection has been obviated. Reconsideration and withdrawal of the objection are respectfully requested.

In the Office Action, claims 1-59 were rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. More specifically, it is asserted that there is no teaching in the prior art regarding known utility of LPAAT-beta inhibitors or their efficacy in any known animal models of disease conditions. Applicants respectfully traverse this rejection.

Submitted herewith by way of Supplemental Information Disclosure Statement (Supplemental IDS) is an article which appeared in Hematological Oncology Today that described work presented at the 14th EORTC-NCI-AACR conference. The article was published in February 2003 which precedes the priority filing date (April 04, 2003) for the subject application. In the article, there is teaching regarding utility of LPAAT-beta inhibitors and their efficacy in animal models of disease conditions. More specifically, it is disclosed that when LPAAT-beta was overexpressed in cell lines, they became more tumorigenic. Further, a small molecule inhibitor specific to LPAAT-beta was used in nude mice bearing HT-29 colon cancer and it significantly delayed tumor growth. In addition, similar results were observed using related compounds in mice with Lewis lung cancers or NCI-H460 human lung cancers. Accordingly, prior to the filing of the subject application, there was teaching regarding utility of

LPAAT-beta inhibitors and their efficacy in animal models of disease conditions. The disclosure of the subject application, especially if taken with the knowledge in the art at the time of the subject invention, provides sufficient guidance for one of ordinary skill in the art to make and use the claimed subject matter without undue experimentation.

Therefore, it is believed that the rejection of claims 1-59 under 35 U.S.C. § 112, first paragraph, has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

In the Office Action, claims 1-59 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants respectfully traverse this rejection.

Claim 1 has been amended as recited above. In order to expedite allowance of certain preferred embodiments of the invention, the heterocyclic forms of the compound of claim 1 have been specified in amended claim 1. Support for the language is found, in part, at page 7, lines 1-8 of the subject application. In claim 1, the term "N₃" refers to an azido group as a substituent and was not intended to define "heterocycle". The term "heterocycle" in claim 1 was not intended to be a choice for "CR₃". In case that was the source of the confusion, "heterocycle" has been moved within the definition of R⁴, R⁵ and R⁶ of claim 1 in order to increase clarity. In addition for further clarity, within the definition of R⁴-R⁶ of claim 1 "CR₃" has been replaced with "CCl₃, CF₃, CBr₃" which are the three recited choices in the claim as originally filed.

Claims 9, 18, 29, 40, 50 and 59 have been amended to recite specific compounds within the elected subject matter.

Claim 19 has been objected to as indefinite. Claim 19 is directed to both in vitro and in vivo methods (see claim 20 and page 15, lines 1-2, of the subject application). The term "reduce" in claim 19 has its ordinary dictionary definition of to lessen in amount. The term is used in claim 19 in the phrase "reduce LPAAT-β activity". In that context, it means any LPAAT-β activity value less than the value prior to contact with a compound or composition of the present invention. The LPAAT-β enzyme resides in cells of tissues, and this is known to those in the art. As described in the above discussion of the February 2003 article submitted

herewith, it was known for example that when LPAAT- β is overexpressed in cells, they become more tumorigenic. To reduce the LPAAT- β activity is beneficial.

As set forth above, claims 20 and 31 have been amended to enhance the clarity. Support for the amendment is found, in part, at page 3, lines 1-11, of the subject application. Claims 20 and 31 now specify that LPAAT- β resides in tissues of an animal.

Claim 30 has been objected to as indefinite. Claim 30 is directed to both in vitro and in vivo methods (see claim 31 and page 15, line 17, of the subject application). The term "inhibiting" refers to both total and partial inhibition (see page 15, lines 20-22, of the subject application). Tumor cells are an example of a cell whose proliferation is desired to be inhibited; however, as described in the subject application (see page 15, lines 17-20), there are cell types other than tumor cells. The end result of inhibiting proliferation is to reduce or eliminate the overgrowth of the cells.

Claim 41 was objected to as indefinite for the use of the term "cancer". As described in the subject application and the February 2003 article submitted herewith, the enzyme is overexpressed (increased activity) in a variety of cancers, not just a single type of cancerous tissue.

Claim 42 was objected to as redundant with claim 41. At page 15, lines 3-12, of the subject application, a representative list of examples of animals is disclosed. Animals in the list that are not mammals include birds and fish.

Claim 51 was objected to on the same basis as claim 30. Accordingly, the discussion above regarding claim 30 is incorporated by reference here in response to the objections to claim 51. In addition, the term "coated medical device" was objected to in claim 51. As disclosed in the subject application, a compound or composition of the present invention may be coated on a variety of medical devices, such as a stent. The medical device need not be of a particular form; it is the nature of the compounds and their uses, as disclosed in the subject application, that are important. The medical device may be used, for example, to inhibit the proliferation of cells, such as tumor cells.

Therefore, it is believed that the rejection of claims 1-59 under 35 U.S.C. § 112, second paragraph, has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

In the Office Action, claims 1-3, 8, 10-12, 17, 30-34, 39, 41-44, 49, 51-53 and 58 were rejected under 35 U.S.C. § 102(b) as unpatentable over Zimmerman et al. (Arch. Pharm. Pharm. Med. Chem. 329:371-376, 1996). In particular, the Examiner drew Applicants' attention to compounds 37 and 38 at page 373 of Zimmerman et al. Applicants respectfully traverse this rejection.

As set forth above, amended claim 1 (and thus claims 2-3, 8, 10-12, 17, 30-34, 39, 41-44, 49, 51-53 and 58 which depend from claim 1 or incorporate the compounds of claim 1 by reference) does not allow for R¹ to be hydrogen. Accordingly, the pending claims of the subject application do not read on the compounds of Zimmerman et al. Applicants further point out that Zimmerman et al. teaches that the compounds disclosed therein are inhibitors of protein kinase C, whereas as recited in the subject application, the compounds of the present invention are inhibitors of LPAAT-β.

Therefore, it is believed that this rejection of the above-identified claims over Zimmerman et al. has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

In the Office Action, claims 1, 2, 8, 10, 11 and 17 were rejected under 35 U.S.C. § 102(b) as unpatentable over Haviv et al. (J. Med. Chem. 26:218-222. 1983). In particular, the Examiner drew Applicants' attention to compound 2J in Table II at page 219 of Haviv et al. Applicants respectfully traverse this rejection.

As set forth above, amended claim 1 (and thus claims 2, 8, 10, 11 and 17 which depend from claim 1 or incorporate compounds of claim 1 by reference) does not allow for R¹ to be hydrogen. Accordingly, the pending claims of the subject application do not read on the compounds of Haviv et al. Applicants note that Haviv et al. provides no teaching that the compounds disclosed therein are inhibitors of LPAAT-β.

Therefore, it is believed that this rejection of claims 1, 2, 8, 10, 11 and 17 over Haviv et al. has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

In the Office Action, claims 1-3 were rejected under 35 U.S.C. § 102 (b) as unpatentable over compound RN 19933-09-6 which is disclosed in Fusco et al. (Gazzeta Chimica Italiana 98:511-534, 1968). As the article of Fusco et al. was published in Italian, Applicants provide herewith an English translation of Fusco et al. in the Supplemental IDS submitted herewith. Applicants respectfully traverse this rejection.

As set forth above, amended claim 1 (and thus claims 2-3 which depend from claim 1) does not allow for R¹ to be hydrogen. Accordingly, the pending claims of the subject application do not read on the compounds of Fusco et al. Applicants note that Fusco et al. provides no teaching that the compounds disclosed therein are inhibitors of LPAAT-β.

Therefore, it is believed that this rejection of claims 1-3 over Fusco et al. has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

In the Office Action, claims 1-2 were rejected under 35 U.S.C. § 102(b) as unpatentable over compound RN 34891-38-8 which is disclosed in Prostakov et al. (Khimiya Geterotsiklicheskikh Soedinenii 7:1137-1138, 1971). Applicants provide herewith a published English translation of Prostakov et al. in the Supplemental IDS submitted herewith. Applicants respectfully traverse this rejection.

As set forth above, amended claim 1 (and thus claim 2 which depends from claim 1) does not allow for R¹ to be hydrogen. Accordingly, the pending claims of the subject application do not read on the compounds of Prostakov et al. Applicants note that Prostakov et al. provides no teaching that the compounds disclosed therein are inhibitors of LPAAT-β.

Therefore, it is believed that this rejection of claims 1-2 over Prostakov et al. has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

In the Office Action, claims 1-3 were rejected under 35 U.S.C. § 102(e) as unpatentable over compound RN 54396-39-2 which is disclosed in Bo et al. (WO 2003/049702). Applicants respectfully traverse this objection.

As set forth above, amended claim 1 (and thus claims 2-3 which depend from claim 1) does not allow for R¹ to be hydrogen. Accordingly, the pending claims of the subject application do not read on the compounds of Bo et al. Applicants note that Bo et al. provides no teaching that the compounds disclosed therein are inhibitors of LPAAT- β .

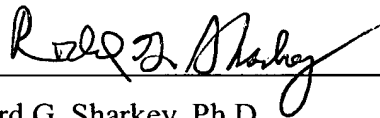
Therefore, it is believed that this rejection of claims 1-3 over Bo et al. has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

Therefore, in light of the amendments and remarks set forth above, Applicants believe that all the Examiner's objections and rejections have been obviated and overcome, respectively. Reconsideration and allowance of the now pending claims (1, 3-10, 12-21, 23-32, 34-42, 44-51 and 53-59) are respectfully requested. If there is any further matter requiring attention prior to allowance of the subject application, the Examiner is respectfully requested to contact the undersigned attorney (at 206-622-4900) to resolve the matter.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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Enclosures:

Extension of Time Petition
Supplemental IDS
PTO-1449 (1 sheet)
Cited References (3)